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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/683,576	10/10/2003	Stephen F. Vatner	601-1-137	9455

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EXAMINER	
MONDESI, ROBERT B	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 01/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/683,576	VATNER ET AL.	
	Examiner	Art Unit	
	Robert B. Mondesi	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 November 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3 and 5-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 5-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Office action is in response to the amendment filed November 21, 2005.

Claims 1-3 and 5-17 are presently pending and under examination.

Withdrawal of Objections and Rejections

The objections and rejections not explicitly restated below are withdrawn.

Maintenance of rejections

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-3 and 5-17 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating cardiac disease in a mammal comprising administering to said mammal an effective amount of a compound selected from the group consisting of dominant negative Mst1 (K594) and XIAP wherein said compound inhibits Mst1, does not reasonably provide enablement for a method of treating cardiac disease in a mammal comprising administering to said mammal an effective amount of a compound or agent that blocks or otherwise inhibits Mst1 or Mst1 pathway. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Claims 1-3, 5-6, 8-10 and 13-14 remain rejected under 35 U.S.C. 102(a) as being anticipated by Yamamoto et al., 2001.

Claims 1-3 and 5-15 remain rejected under 35 U.S.C. 102(b) as being anticipated by Han et al., US Patent No: 6,225,288.

Claims 1-3, 7-9 and 13-14 remain rejected under 35 U.S.C. 102(e) as being anticipated by Laugwitz et al., US Patent Publication No: 2003/0130216.

Claims 10-12 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Han et al., US Patent No: 6,225,288 in view of Danilewicz et al. US Patent No: 4,975,444.

Claims 15-17 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Han et al., US Patent No: 6,225,288 in view of Kukreja US Patent Pub. No: 2004/0009957.

The above rejections were explained in the Office action.

Response to applicant's arguments

In regards to the rejection of the **claims 1-3 and 5-17** under 35 U.S.C. 112, first paragraph, applicants assert that the Specification describes and details the effectiveness of Mst1 inhibitors, including a dominant negative mutant of Mst1 and a chemical agent XIAP. In addition, the Specification, at page 54 paragraph (0158, describes that phosphorylation regulates (activates) Mst1 activity and that a C-terminal inhibitory domain of Mst1 affects Mst1. Applicants assert further that the skilled artisan can readily identity compounds or agents, including other Mst1 dominant negative mutants and specific Mst1 inhibitors, and can test their ability to inhibit endogenous Mst1 and to thereby modulate cardiac myocyte apoptosis or function, for use in the

claimed methods. While experimentation is necessary, it is not undue and well within the capability of the skilled artisan, particularly taking into account the teaching of the Specification and the knowledge publicly available regarding Mst1.

Applicants' arguments have not been found persuasive. In response to applicant's argument that the specification describes and details effectiveness of Mst1 inhibitors, it is noted that the features upon which applicant relies (i.e., a chemical agent XIAP and a C-terminal inhibitory domain) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Furthermore, the applicants have acquiesced on the record that "with regards to the claimed invention further experimentation is necessary"; although, consider it to be NOT undue by those skill in the art. It must be noted that the issue in this case is the breath of the claims in light of the predictability of the art as determined by the number of working examples, the skill level of the artisan and the guidance presented in the instant specification and the prior art of record. The Applicants make and test position is inconsistent with the decisions of *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) where it is stated that "... scope of claims must bear a reasonable correlation to scope of enablement provided by the specification to persons of ordinary skill in the art...". Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily and improperly extensive and undue. See *In re Wands*, 858

F.2d at 737, 8 USPQZd at 1404 (Fed. Cir. 1988). Therefore, for the instant specification to be enabling, it needs to provide direction/guidance regarding a sufficient amount of the compounds or agents that block or otherwise specifically inhibit Mst1. Absent sufficient guidance/direction one of skill in the art would not be able to practice the claimed invention commensurate in scope with the claims.

In regards to the rejection of the **claims 1-3, 5-6, 8-10 and 13-14** remain rejected under 35 U.S.C. 102(a) as being anticipated by Yamamoto et al., 2001 applicants assert that Yamamoto does not teach or describe anything with regard particularly to Mst1 and anticipation is a question of fact. Applicants have cancelled claim 4 and amended claims 1, 3, 8, 9, 10, 13 and 14 in order to clarify the language of the claims and to direct the claims more particularly to the invention and to uses of specific inhibitors of Mst1. Applicants assert that the above amendments obviate this rejection.

Applicants' arguments have not been found persuasive. The method of the invention is a method of treating cardiac disease in mammal that comprises the administering of Mst1 inhibitors and on page 27, lines 22-24 of the specification applicants have clearly stated that "the inhibitor can include, but is not limited to the specifically identified Capase 3, Calyculin A and Chelerythrine". As indicated previously in Office action mailed May 20, 2005, Yamamoto et al. teach the administering of Chelerythrine (Page 1846, column 1, lines 2-8). Furthermore the applicants have not explained or clarified what is meant by "specifically inhibits". It is not clear as to what the difference between compounds that specifically inhibit and compounds that non-

specifically inhibit is supposed to be (this statement applies to all the responses and assertions below).

In regards to the rejection of **claims 1-3 and 5-15** under 35 U.S.C. 102(b) as being anticipated by Han et al., US Patent No: 6,225,288, applicants assert that Han et al. do not teach or describe anything with regard particularly to Mst1 and anticipation is a question of fact. Applicants have above cancelled claim 4 and amended claims 1, 3, 8, 9, 10, 13 and 14 in order to clarify the language of the claims and to direct the claims more particularly to the invention and to uses of specific inhibitors of Mst1. Applicants assert that the above amendments obviate this rejection.

Applicants' arguments have not been found persuasive. The method of the invention is a method of treating cardiac disease in mammal that comprises the administering of Mst1 inhibitors and on page 27, lines 22-24 of the specification applicants have clearly stated that "the inhibitor can include, but is not limited to the specifically identified Caspase 3, Calyculin A and Chelerythrine". As indicated previously in Office action mailed May 20, 2005, Han et al. teach the administering of Caspase 3 (Column 83, lines 42-47).

In regards to the rejection of **claims 1-3, 7-9 and 13-14** under 35 U.S.C. 102(e) as being anticipated by Laugwitz et al., US Patent Publication No: 2003/0130216, applicants assert that Laugwitz et al. do not teach or describe anything with regard particularly to Mst1 and anticipation is a question of fact. Applicants have above cancelled claim 4 and amended claims 1, 3, 8, 9, 10, 13 and 14 in order to clarify the language of the claims and to direct the claims more particularly to the invention and

to uses of specific inhibitors of Mst1. Applicants assert that the above amendments obviate this rejection.

Applicants' arguments have not been found persuasive. The method of the invention is a method of treating cardiac disease in mammal that comprises the administering of Mst1 inhibitors and on page 27, lines 22-24 of the specification applicants have clearly stated that "the inhibitor can include, but is not limited to the specifically identified Caspase 3, Calyculin A and Chelerythrine". As indicated previously in Office action mailed May 20, 2005, Laugwitz et al. teach the the administering of Caspase 3 (Page 2, column 2, lines 12-12 and section 0010, lines 1-6).

In regards to the rejection of **claims 10-12** under 35 U.S.C. 103(a) as being unpatentable over Han et al., in view of Danilewicz et al. and **claims 15-17** under 35 U.S.C. 103(a) as being unpatentable over Han et al., in view of Kukreja, applicants simply assert that the combination of Han and Danilewicz does not teach or suggest the use or combination of specific Mst1 inhibitors with any other compounds for treatment of cardiac disease. In particular and in view of the above claim amendments, particularly in claims 10 and11, the combination of Han and Danilewicz does not make obvious the claimed invention and also the combination of Han and Kukreja does not teach or suggest the use or combination of specific Mst1 inhibitors with any other compounds for treatment of cardiac disease. In particular and in view of the above claim amendments, particularly in claims 11, 13, 14 and 15, the combination of Han and Kukreja does not make obvious the claimed invention.

Applicants' arguments have not been found persuasive. The mentioned combinations of references cited by the examiner, do indeed render the mentioned claims obvious, as indicated in Office action mailed May 20, 2005, and for reasons stated above. Applicants have not provided any specific assertions that would refute examiners rejections of **claims 10-12 and 15-17** under 35 U.S.C 103 (a); however for the purpose of closure and completeness the following previously submitted assertions are restated: It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine Han et al. and Danilewicz et al. because, "It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose....[T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980) (citations omitted) and It would have been obvious to one of ordinary skill in the art at the time the invention was made to co-adminiter an inhibitor of Mst1 with doxorubicin for the advantages lessening the occurrence of Doxorubicin-induced cardiotoxicity as taught by Han et al. and Kukreja, see Kureja at Section 0047, Lines, 15-19.

New Objection(s) and Rejection(s)

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3 and 5-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants have amended **claim 1** in order to include the new limitation "specifically" and therefore presently the invention is drawn to a method that specifically inhibits Mst1; however nowhere in the specification of the present application is it disclosed or described what is meant by specifically inhibiting Mst1 in view of the method of invention, which is a method of treating cardiac disease in a mammal. Accordingly, the new limitation is considered to be new matter since the specification of the specification lacks support for the mentioned limitation. **Claims 2-3 and 5-17** are dependent claims that do not remedy the deficiencies of the independent claim that they depend therefrom.

Claims 1-3 and 5-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicants have amended **claim 1** to include the term "specifically" and **claims 10-11 and 15** to include the term "specific", as a new claim limitation; however the

applicants have not explained or clarified, in specification of the present application or anywhere in the dependent claims, what is meant by "specifically" inhibits or "specific" Mst1 inhibitor. It is not clear as to what the difference between compounds that specifically inhibit and compounds that non-specifically inhibit, is supposed to be and how the terms specifically and specific are supposed to further limit the claims to certain compounds and agents. **Claims 2-3, 5-9, 12-14 and 16-17** are dependent claims that do not remedy the deficiencies of the independent claim that they depend therefrom.

Conclusion

No claims are allowed

Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert B Mondesi whose telephone number is 571-272-0956. The examiner can normally be reached on 9am-5pm, Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Group 1653
1-18-05

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SUPERVISORY PATENT EXAMINER